REMARKS

Applicants have amended claims 11, 23 and 30 to make explicit that which has been implicit, namely that the target sequences of the present arrays contain a unique 3' end, i.e. the end extending to the z-dimension, and that the target sequences are separated by sequences that are the same, generic sequences. These amendments are supported throughout the specification and figures.

At page 10, lines 15-18, the specification states

"circular DNA template comprising i) a region having **a sequence complementary to at least a portion of said generic oligonucleotide** (shown in Figure 1A as AAAACC), and ii) a region comprising a **sequence of interest**...".

By amplifying such a circular template towards the z-dimension on an array, one necessarily ends up with an array that has a target sequence separated by an identical generic sequence.

At page 11, lines 19-23, the specification states

"each oligonucleotide comprises a region comprising **a different sequence** (Figure 1B is merely illustrative, showing one such oligonucleotide with one such **unique sequence**), each different sequence being complementary to a sequence of interest on a circular template. The circular DNA template comprises i) a first region (shown in Figure 1B as ACGATAAAACC) and ii) **a second region** (shown in Figure 1B as QQQQetc.)..."

Accordingly, by amplifying such a circular template towards the z-dimension on a array, one necessarily ends up with an array that has the unique sequences separated by a second, identical sequence.

Claims 24-29 and 31-33 have been amended accordingly.

Turning now to the specific objections and rejections of the claims.

The Examiner objected to claims 11 and 23 because of the use of the infinite article "a" before the adjective "unique." The Applicants respectfully submit that according to the English grammar rules, the infinite article "a" is used before a word that begins with the vowel "u" when "u" sounds like 'you.' The word "unique" is one such word. Accordingly, the claims are correct

in using an infinite article "a" instead "an" and the objection should be withdrawn. Exhibit A regarding the grammar rule is attached.

The Examiner rejected claims 11 and 23-38 under 35 U.S.C. §112 first paragraph as allegedly containing new matter.

The Applicants respectfully disagree and request that the rejection be withdrawn for the following reasons.

The array of the present invention is prepared by a method, as described in the present application, that cannot produce an array other than one wherein one ends up with a unique end at the z-dimension **which is the 3' direction of the extended template because the nucleic acid synthesis using polymerases always advances in 5' to 3' direction (also, see, Figure 3A)** for each amplified template. Figures 1A and 1B show that the DNA binds to the array at the 5' end and is extended by a circular DNA template ending at the 3' end. This methodology creates a unique 3' end for each probe. This is further explained by the text. For example, at page 10:

> The method contemplates a solid support with positions for oligonucleotides defined by x and y coordinates... Each circular DNA template is added under conditions such that the circular DNA template hybridizes with the generic immobilized oligonucleotide, said immobilized oligonucleotide thereafter being extended by a polymerase to create a unique extended nucleic acid strand at each position on the solid support, such extended strands comprising two or more (and more typically three or more, and more preferably, ten or more, and still more preferably more than fifty) copies of the sequence of interest. Thereby, an array is created with redundancy in the z dimension (i.e., out of the x and y plane of the solid support).

The specification goes on to talk about variations in the circular template. Thus a number of embodiments of the z strand are shown. All contain the gene of interest. In one embodiment, between each target sequence repeat there is either a sequence that is complementary to at least a portion of the oligonucleotide that attaches the sequence to the array (claim 11) or some other standard sequence (claim 23). This is achieved, as claimed, by having "a plurality of unique circular DNA templates, each circular DNA template comprising a sequence of interest and a region complementary to at least a portion of said sequence of said oligonucleotide, said sequence of interest **being different for each circular DNA template**.

35 U.S.C. § 112, first paragraph, requires a written description of the invention which is separate and distinct from the enablement requirement. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). The proper test for sufficiency of description in a patent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983). Exactly how the specification allows one skilled in the art to recognize that an applicant had possession of the claimed invention is not material. In re Smith, 481 F. 2d 910, 178 USPQ 279 (CCPA 1973). Typically, an applicant conveys that he or she is in possession of the invention by use of descriptive means such as "**words**, structures, **figures**, diagrams, formulas, etc., that set forth the claimed invention." Lockwood v. American Airlines, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). [Emphasis added]. To comply with the description requirement, it is not necessary that the application describe the invention ipsis verbis . In re Lukach, 442 F.2d 967, 169 USPQ 795 (CCPA 1971). What is required is that an ordinarily skilled artisan recognize from the disclosure that applicants invented the subject matter of the claims, including the limitations recited therein. Smith, 481 F. 2d at 915, 178 USPQ at 284. The burden of showing that the claimed invention is not described in the specification rests on the PTO in the first instance, and it is up to the PTO to give reasons why a description not in ipsis verbis is insufficient. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). Determining whether the written description requirement is met involves a factual inquiry insofar as determining how close the original description must come to the recitation in the claim(s). See Eiselstein v. Frank, 52 F.3d 1035, 1039, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995); In re Driscoll, 562 F.2d 1245, 1250, 195 USPQ2d 434,438 (CCPA 1977). This interpretation still holds (Union Oil Co. of California v. Atlantic Richfield Co. , 208 F3d 989, 54 USPQ2s 1227; (Fed. Cir. 2000)).

Accordingly, Applicants submit that the claims clearly comply with the 35 U.S.C. §112, first paragraph. Nevertheless, the further amendments have obviated such rejections. Accordingly, in view of the foregoing, the rejection should be withdrawn.

Claims 11 and 23-38 were rejected under 35 U.S.C. §102(e) as being anticipated by Smith et al., U.S. Patent No. 5,753,439, filed May 19, 1998 ("Smith").

Applicants respectfully submit that the arrays of Smith are substantially different from the claimed arrays.

Applicants submit that the product of the present invention differs from the product of Smith in that the oligonucleotide probes in the arrays of the present invention have been extended at their 3' termini thus resulting in differing 3' termini according to the sequence of interest. The **3' terminus** of each strand of the **Smith array** is always **the same**. The array of Smith comprises oligonucleotide probes that "comprise 5'-region and 3'regions which are complementary to portions of the nucleic acid and an internal variable region" (col. 7, lines 3-5). Even if this variable region comprises multiple repeats of a same target sequence, the middle part of the probe is always flanked by the 3' and 5' sequences that do not belong to the target sequence. This means that each probe has 100% identical 5' ends and 100% identical 3' ends, and a variable region in between. This is not the same with the claimed arrays.

The array of claim 11, can have 100% identical 5'end (each oligo attached to the surface can be the same generic oligonucleotide) but the rest of the probe comprises a repeat that comprises a target sequence and a portion of the sequence complementary to the that standard oligo attached to the array. Unlike in the probes of the arrays of Smith, there is no difference in the sequence at the end of the variable region of the probe from the internal variable region, and therefore the 3' end of each probe is unique. Smith requires a 5' constant region – a variable internal region – a 3' constant region. Based upon the present claim and the use of a circular array-forming method, the 3' end of each probe differs from that of Smith. For example, the circular template is repeated at least twice, at least ten time (e.g. claims 25 and 28) at least 50 times (e.g. claims 26 and 29). By using the circular template, the 3' terminus differs from that of Smith.

In claim 32, the probes are similarly homeogenous towards the z dimension, i.e. the 3' end of the probe. The difference being that the 5'end of the each of the probe comprises a sequence that is unique and when a circular template that has a sequence complementary to at least a portion of the unique sequence attaches to the unique original probe, an array will be created that again has a repeat with unique sequence followed by a second region, followed by a second copy of the unique sequence and so forth. Again, unlike in the probes on the arrays of

Smith, there will be no separate region at the end of the variable region of each probe, and therefore the 3' end of each probe is unique.

Accordingly, in light of the above, Applicants submit that the rejection under 35 U.S.C. §102(e) should be withdrawn.

In view of the foregoing, applicants submit that all claims are in condition for allowance. Early and favorable action is requested.

Respectfully submitted,

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